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Term	Documents
"HER.BETA".DWPI,TDBD,EPAB,JPAB,USPT,PGPB.	1
HER.BETAS	0
HER	0
HER.S	0
BETA.	0
"BETA.S".DWPI,TDBD,EPAB,JPAB,USPT,PGPB.	352
(("HER." ADJ "BETA.") OR "HER.BETA").USPT,PGPB,JPAB,EPAB,DWPI,TDBD.	1

US Patents Full-Text Database
 US Pre-Grant Publication Full-Text Database
 JPO Abstracts Database
 EPO Abstracts Database
 Derwent World Patents Index
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Database:

her.beta or her. beta.

[Refine Search:](#)[Clear](#)**Search History****Today's Date: 5/18/2001**

<u>DB Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u>
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	her.beta or her. beta.	1	<u>L4</u>
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	herbeta or her-beta or her beta	4	<u>L3</u>
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	human estrogen receptor	252	<u>L2</u>
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	estrogen receptor	1674	<u>L1</u>

FILE 'MEDLINE'
FILE 'JAPIC'
FILE 'BIOSIS' C) 2001 BIOSIS(R)

FILE 'SCISEARCH'
FILE 'WPIDS'
FILE 'CAPLUS'
FILE 'EMBASE'
=> s estrogen receptor#

5 FILES SEARCHED..
L1 79174 ESTROGEN RECEPTOR#

=> s II and (her beta or her-beta or herbeta or her beta or her beta.)

5 FILES SEARCHED..
L2 43 L1 AND (HER BETA OR HER-BETA OR
HERBETA OR HER.BETA OR HER.
BETA.)

=> dup rem l2

PROCESSING COMPLETED FOR L2
L3 13 DUP REM L2 (30 DUPLICATES REMOVED)

=> d l3 ibib abs 1-13

L3 ANSWER 1 OF 13 WPIDS COPYRIGHT 2001
DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-168581 [17] WPIDS
DOC. NO. NON-CPI: N2001-121530
DOC. NO. CPI: C2001-050401
TITLE: Determination of the interaction of a substance for investigation and diagnosis of hormonal disorders

using an optically labelled receptor protein.

DERWENT CLASS: B04 D16 S03
INVENTOR(S): KATO, N.; SAKAMOTO, H.
PATENT ASSIGNEE(S): (OLYU) OLYMPUS OPTICAL CO LTD

COUNTRY COUNT: 8

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2001007919 A1 20010201 (200117)* JA 75
RW: DE FI FR GB NL SE
W: JP US

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001007919 A1	WO 2000-JP4930	20000724	

PRIORITY APPLN. INFO: JP 2000-163476 20000531; JP 1999-209860

19990723, JP 2000-163475 20000531

AN 2001-168581 [17] WPIDS

AB WO 200107919 A UPAB: 20010328

NOVELTY - Examination of the interaction of a test substance with a hormone receptor protein is new.

DETAILED DESCRIPTION - The method comprises:

(a) the test substance is contacted with a hormone receptor protein labelled with a marker which generates an optical signal under conditions

in which the receptor protein can bind to a ligand and after binding undergo a change of state so as to alter the properties of the optical signal;

(b) the optical signal is detected under these conditions; and

(c) the optical signal produced is compared with that generated in the absence of the test substance, to show whether the test substance is interacting with the hormone receptor protein.

INDEPENDENT CLAIMS are also included for:

(1) genes encoding the labelled hormone receptor protein;

(2) vectors containing the genes;

(3) host cells transformed by the vectors; and

(4) the labelled hormone receptor protein.

USE - Investigation and diagnosis of hormonal disorders especially those of sex hormones such as suppression of ovulation.

DESCRIPTION OF DRAWING(S) - The drawing shows the fluorescence correlation spectroscopy traces of a green fluorescent protein/human

estradiol receptor beta fusion protein at the time of addition of

estradiol and after 45 minutes from addition - the shift in the

trace shows that interaction of the hormone and receptor is taking place.
(Drawing includes non-English language text).
Dwg.14/14

L3 ANSWER 2 OF 13 SCISEARCH COPYRIGHT 2001 ISI

(R) DUPLICATE 1
ACCESSION NUMBER: 2001:165025 SCISEARCH

THE GENUINE ARTICLE: 401HB

TITLE: Unique protein determinants of the subtype-selective

ligand responses of the ***estrogen***
receptors (ER alpha and ER beta) at AP-1 sites

AUTHOR: Weatherman R V; Scanlan T S (Reprint)

CORPORATE SOURCE: Univ Calif San Francisco, Dept

Pharmaceut Chem, San Francisco, CA 94143 USA (Reprint); Univ Calif

San Francisco, Dept Cellular Mol Pharmacol, San

Francisco, CA 94143 USA

COUNTRY OF AUTHOR: USA

SOURCE: JOURNAL OF BIOLOGICAL

CHEMISTRY, (9 FEB 2001) Vol. 276,

No. 6, pp. 3827-3832.

Publisher: AMER SOC BIOCHEMISTRY

MOLECULAR BIOLOGY INC,

9630 ROCKVILLE PIKE, BETHESDA, MD

20814 USA

ISSN: 0021-9258.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 38

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The two subtypes of human ***estrogen***

receptor, alpha

(hER alpha and beta (***hER*** ***beta***),

regulate transcription

at an AP-1 response element differently in response to

estradiol and the

anti-estrogens tamoxifen and raloxifene. To better

understand the protein

determinants of these differences, chimeric and deletional

mutants of the

N-terminal domain and the F region of ER alpha and ER

beta were made and

tested in transient transfection assays at the classical

estrogen response

element (ERE) site as well as at an AP-1 site. Although the

same regions

on each receptor subtype appeared to be primarily

responsible for

estradiol activation at an ERE and in HeLa cells, major

differences

between ER alpha and ER beta mutants were seen in the

estrogen and

anti-estrogen responses at an AP-1 site. This differential

ligand response

maps to the N-terminal domain and the F region. These

results suggest that

different estrogenic and anti-estrogenic ligands use different

mechanisms

of activation and inhibition at the AP-1 site. In contrast to

previous

studies, this work also shows that many of subtype-specific

responses are

not transferred to the other subtype by swapping the

N-terminal domain of

the receptor. This implies that there are other unique

surfaces presented

by each subtype outside of the N-terminal domain, and

these surfaces can

play a role in subtype-selective signaling. Together, these

data suggest a

complex interface between ligand, response element, and

receptor that

underlies ligand activation in estrogen signaling pathways.

L3 ANSWER 3 OF 13 SCISEARCH COPYRIGHT 2001 ISI

(R) DUPLICATE 2

ACCESSION NUMBER: 2001:294637 SCISEARCH

THE GENUINE ARTICLE: 416UG

TITLE: Interaction of phytoestrogens with

estrogen

receptors alpha and beta

AUTHOR: Morito K; Hirose T; Kinjo J; Hirakawa T;

Okawa M; Nohara T; Ogawa S; Inoue S; Muramatsu M; Masamune

Y (Reprint)

CORPORATE SOURCE: Kanazawa Univ, Fac Pharmaceut

Sci, Dept Mol & Cellular

Biol, 13-1 Takara Machi, Kanazawa, Ishikawa

9200934, Japan

(Reprint); Kanazawa Univ, Fac Pharmaceut Sci,

Dept Mol &

Cellular Biol, Kanazawa, Ishikawa 9200934,

Japan; Fukuko Univ, Fac Pharmaceut Sci, Lab Pharmacognosy,

Fukuoka

8140180, Japan; Kumamoto Univ, Fac

Pharmaceut Sci, Lab Nat Med, Kumamoto 8620973, Japan; Univ Tokyo,

Grad Sch Med,

Dept Geriatr Med, Bunkyo Ku, Tokyo 1138655, Japan; Saitama

Med Sch, Dept Biochem, Moroyama, Saitama 3500451, Japan

COUNTRY OF AUTHOR: Japan

SOURCE: BIOLOGICAL & PHARMACEUTICAL

BULLETIN, (APR 2001) Vol. 24,

No. 4, pp. 351-356.

Publisher: PHARMACEUTICAL SOC JAPAN, 2-12-15-201 SHIBUYA,

SHIBUYA-KU, TOKYO, 150, JAPAN.

ISSN: 0918-6158.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 37

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The human ***estrogen*** ***receptor*** (hER) exists as two

subtypes, hER alpha and ***hER*** ***beta***, that differ in the C-terminal ligand-binding domain and in the N-terminal transactivation

domain. In this study, we investigated the estrogenic activities of soy

isoflavones after digestion with enteric bacteria in competition binding

assays with hER alpha or ***hER*** ***beta***

protein, and in a

gene expression assay using a yeast system. The estrogenic activities of

these isoflavones were also investigated by the growth of MCF-7 breast cancer cells.

Isoflavone glycoside binds weakly to both receptors and ***estrogen*** ***receptor*** -dependent transcriptional expression

is poor. The aglycones bind more strongly to ***hER*** ***beta***

than to hER alpha. The binding affinities of genistein, dihydrogenistein

and equol are comparable to the binding affinity of 17 beta-estradiol.

Equol induces transcription most strongly with hER alpha and ***hER***

beta. The concentration required for maximal

gene expression is

much higher than expected from the binding affinities of the compounds,

and the maximal activity induced by these compounds is about half the

activity of 17 beta-estradiol. Although genistein binds more weakly to the receptors and induces transcription less than does genistein, it

stimulates the growth of MCF-7 cells more strongly than does genistein.

L3 ANSWER 4 OF 13 MEDLINE

DUPLICATE 3

ACCESSION NUMBER: 2001204445 MEDLINE

DOCUMENT NUMBER: 21111546 PubMed ID: 11158716

TITLE: Hydroxylated benzo[a]pyrene metabolites are responsible for

in vitro ***estrogen*** ***receptor***

-mediated gene expression induced by benzo[a]pyrene, but do not

elicit uterotrophic effects in vivo.

AUTHOR: Fertuck K C; Matthews J B; Zacharewski T R

CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Michigan

State University, Lansing, Michigan 48824, USA.

SOURCE: TOXICOLOGICAL SCIENCES, (2001 Feb)

59 (2) 231-40.

Journal code: CZ1; 9805461. ISSN: 1096-6080.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200104

ENTRY DATE: Entered STN: 20010417

Last Updated on STN: 20010417

Entered PubMed: 20010222

Entered Medline: 20010412

AB The estrogenic activities of benzo[a]pyrene (B[a]P) and 10 metabolites (I,

3-, 7-, and 9-hydroxy-B[a]P; 4,5-, 7,8-, and

9,10-dihydroxy-B[a]P;

and 1,6-, 3,6-, and 6,12-B[a]P-dione) were investigated. In

vitro,

B[a]P did not displace tritiated 17beta-estradiol ([3H]E2) from

either a bacterially expressed fusion protein consisting of glutathione-S-

transferase linked to the D, E, and F domains of human ERalpha (GST-hERalphadef), or from full-length human ERbeta (***hERbeta***) at concentrations as high as 60 microM. However, 10 microM B[a]P demonstrated partial agonist activity in human Gal4-ERalphadef and mouse Gal4-ERbetadef reporter gene assays in transiently transfected MCF-7 cells, relative to 10 nM E2. 1-, 3-, 7-, and 9-hydroxy-B[a]P were found to bind to both receptor isoforms, each showing a higher affinity for the beta isoform. At 10 microM the four monohydroxylated metabolites were able to induce Gal4-hERalphadef- and Gal4-mERbetadef-mediated reporter gene expression to levels 20-100% of that caused by 10 nM E2, suggesting that these metabolites, and not the parent compound, induced reporter gene expression following B[a]P treatment of transiently transfected MCF-7 cells. In addition, the effect of B[a]P on two estrogen-inducible end points, uterine weight and lactoferrin mRNA levels, was determined in ovariectomized DBA/2 and C57BL/6 mice. Neither orally administered B[a]P at doses as high as 10 mg/kg body weight nor subcutaneously injected 3- or 9-hydroxy-B[a]P at doses as high as 20 mg/kg induced effects on uterine wet weight or uterine lactoferrin mRNA levels in either strain. These data suggest that B[a]P metabolites that are estrogenic at high concentrations in vitro do not induce estrogenic effects in the mouse uterus.

L3 ANSWER 5 OF 13 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 4
ACCESSION NUMBER: 2001:148981 BIOSIS DOCUMENT NUMBER: PREV200100148981
TITLE: In vitro and in vivo interactions of bisphenol A and its metabolite, bisphenol A glucuronide, with ***estrogen*** ***receptors*** alpha and beta.
AUTHOR(S): Matthews, Jason B.; Twomey, Ken; Zacharewski, Timothy R.

(I)
CORPORATE SOURCE: (1) Department of Biochemistry and Molecular Biology, Michigan State University, Wilson Road, 223 Biochemistry Building, East Lansing, MI, 48842-1319.
tzachare@pilot.msu.edu USA

SOURCE: Chemical Research in Toxicology, (February, 2001) Vol. 14, No. 2, pp 149-157. print.
ISSN: 0893-228X.
DOCUMENT TYPE: Article
LANGUAGE: English

SUMMARY LANGUAGE: English
AB: The estrogenic activities of bisphenol A (BPA) and its major metabolite BPA glucuronide (BPA-G) were assessed in a number of in vitro and in vivo assays. BPA competed with (3H)-17beta-estradiol (E2) for binding to mouse uterine cytosol ER, a glutathione S-transferase (GST)-human ER D, E, and F domain fusion protein (GST-hERalphadef) and full-length recombinant ***hERbeta*** . The IC50 values for E2 were similar for all three receptor preparations, whereas BPA competed more effectively for binding to ***hERbeta*** (0.96 muM) than to either mouse uterine cytosol ER (26 muM) or GST-hERalphadef (36 muM). In contrast, BPA-G did not competitively displace (3H)E2 from any of the ER preparations. In MCF-7 cells transiently transfected with Gal4-hERalphadef or Gal4-hERbetadef,

BPA induced reporter gene activity with comparable EC50 values (71 and 39 muM, respectively). No significant induction of reporter gene activity was seen for BPA-G. Cotreatment studies showed that concentrations of (10 muM) BPA and BPA-G did not antagonize E2-induced luciferase mediated through either Gal4-hERalphadef or Gal4-hERbetadef. In vivo, the uterotropism effect of gavage or subcutaneous (sc) administration of 0.002-800 mg of BPA/kg of body weight/day for three consecutive days was examined in

immature rats. Dose-related estrogenic effects on the rat uterus were observed at oral doses of 200 and 800 mg/kg and at sc doses of 10, 100, and 800 mg/kg. These results demonstrate that BPA competes more effectively for binding to ERbeta, but induces ERalpha- and ERbeta-mediated gene expression with comparable efficacy. In contrast, BPA-G did not exhibit any in vitro estrogenic activity. In addition, there was a clear route dependency on the ability of BPA to induce estrogenic responses in vivo.

L3 ANSWER 6 OF 13 MEDLINE
ACCESSION NUMBER: 2001129427 MEDLINE
DOCUMENT NUMBER: 21038386 PubMed ID: 11187733
TITLE: Phytoestrogens.
AUTHOR: Kinjo J
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Fukuoka University.
SOURCE: NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (2000 Dec) 58 (12) 2434-8. Ref. 20 Journal code: KIM; 0420546. ISSN: 0047-1852.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered PubMed: 20010122
Entered Medline: 20010301
AB: Epidemiological studies revealed that foodstuffs, in particular, soy foods containing isoflavonoid phytoestrogens may reduce the risk of some hormone-dependent disease such as not only postmenopausal symptoms but also certain(breast, prostate and colon) cancers and cardiovascular disease. This review introduces the metabolism of soybean isoflavonoids by human intestinal bacteria and the binding and gene-expression activity of the metabolites towards the human ***estrogen*** ***receptor*** (HER) alpha and beta. The dietary isoflavones(daidzin and genistein) in soybean were metabolized to equol and dihydrogenistein via daidzein and genistein, respectively. The metabolites bind more strongly to ***hER*** ***beta*** than hER alpha. The binding affinity of genistein is comparable that of 17 beta-estradiol. Equol induces transcription most strongly both with ***hER*** ***beta*** and hER alpha.

L3 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:139632 CAPLUS
DOCUMENT NUMBER: 133:145672
TITLE: Sequencing and cloning of human estrogen beta.
AUTHOR(S): Huang, Hefeng; Mershon, J. L.; Wang, Jinfu
CORPORATE SOURCE: Women's Hospital, School of Medicine, Zhejiang University, Hangzhou, 310006, Peop. Rep. China
SOURCE: Zhonghua Yixue Zaishi (2000), 80(1), 28-30
CODEN: CHHTAT; ISSN: 0376-2491
PUBLISHER: Zhonghua Yixue Zaishi
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB: Granulosa cells were prep'd. from the ovary of IVF-ET cases by Percoll technique with Dulbecco's modified eagle medium to analyze the nucleotide sequence of cDNA and deduce the amino acid sequence of human ***estrogen*** ***receptor*** (***hER*** ***beta***) in human granulosa cells. RNA was extd. with the TRizol reagent kit, and mRNA was purified with oligo-(dT)-cellulose, and cDNA was prep'd. from the mRNA by PCR. Amplified products were cloned into the pGEM-T vector and transfected into E. coli XL1-Blue. The nucleotide sequence was detd. by the Sequenase Version 2.0 DNA sequencing kit. The cDNA for ***hER*** ***beta*** from human granulosa cells was composed

of 1495 bp, contg. a 1431 bp open reading frame, encoding 477 amino acids. The predicted ER protein included 4 functional domains: A/B, C, D, and E/F. The C domain, richly contg. cysteine, was the DNA-binding domain (DBD), and E/F domain was the ligand-binding domain (LBD) among these domains. Detection of ER beta in the ovary granulosa cells played an important role in explaining the self-endocrine function of estrogen.

L3 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:127018 CAPLUS
DOCUMENT NUMBER: 130:192325
TITLE: Cloning and cDNA sequence encoding a full-length human ***estrogen*** ***receptor*** -beta.
INVENTOR(S): Bhat, Ramesh A.; Henderson, Ruth Ann; Hsiao, Chulai; Karathanasis, Sotrios Konstantinou
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIIXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
PATENT NO. KIND DATE APPLICATION NO.

WO 9907847 A1 19990218 WO 1998-US14944
19980720 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9884988 A1 19990301 AU 1998-84988
19980720 PRIORITY APPLN. INFO.: US 1997-906365
19970805 WO 1998-US14944 19980720
AB: The present invention provides isolated nucleic acids encoding full-length human ***estrogen*** ***receptor*** -beta. (***hER*** ***beta***), which comprises 530 amino acids. The invention also provides isolated ***hER*** ***beta*** polypeptides and ***hER*** ***beta*** -reactive antibodies, including those that specifically recognize amino acids 1-45 of ***hER*** ***beta*** , which were not previously known. An optimal Kozak translation initiation sequence is found upstream of the newly discovered initiator methionine codon, and anal. of expressed transcripts also supports expression of the long isoform. ***hER*** ***beta*** is selectively expressed in the thymus, spleen, ovary, and testes. In the presence of estradiol, ***hER*** beta long form is about 2-3-fold more active than the short form in stimulation of estrogen-response elements in HepG2 cells. The invention also encompasses methods for identifying ***hER*** ***beta*** -interactive compds., including agonists, antagonists, and co-activators.

REFERENCE COUNT: 3
REFERENCE(S): (1) Akzo Nobel Nv; EP 0798378 A 1997 CAPLUS
(2) Karobio, A; WO 9709348 A 1997 CAPLUS
(3) Mosselman, S; Febs Letters 1996, V392(1),

P49 CAPLUS
L3 ANSWER 9 OF 13 MEDLINE
DUPLICATE 5
ACCESSION NUMBER: 1999:174617 MEDLINE
DOCUMENT NUMBER: 99174617 PubMed ID: 10076999
TITLE: ***Estrogen*** ***receptor*** beta activates the human retinoic acid receptor alpha-1 promoter in

response to tamoxifen and other ***estrogen*** receptor*** antagonists, but not in response to estrogen.
 AUTHOR: Zou A; Marschke K B; Arnold K E; Berger E M; Fitzgerald P;
 Mais D E; Allegretto E A
 CORPORATE SOURCE: Department of Retinoid Research, Ligand Pharmaceuticals, Inc., San Diego, California 92121, USA.
 SOURCE: MOLECULAR ENDOCRINOLOGY, (1999 Mar) 13 (3) 418-30.
 Journal code: NGZ; 8801431. ISSN: 0888-8809.
 PUB. COUNTRY: United States
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199905
 ENTRY DATE: Entered STN: 19990517
 Last Updated on STN: 19990517
 Entered Medline: 19990506
 AB Human ***estrogen*** ***receptor*** -alpha (hERalpha) or -beta (***hERbeta***) transfected into Hep G2 or COS1 cells each responded to estrogen to increase transcription from an estrogen-responsive element (ERE)-driven reporter vector with similar fold induction through a classical mechanism involving direct receptor binding to DNA. ER antagonists inhibited this estrogen induction through both hERalpha and ***hERbeta***, although raloxifene was more potent than hERalpha than ERbeta, and tamoxifen was more potent via ERbeta than hERalpha. We have shown previously that estrogen stimulated the human retinoic acid receptor-alpha-1 (hRARalpha-1) promoter through nonclassical EREs by a mechanism that was ERalpha dependent, but that did not involve direct receptor binding to DNA. We show here that in contrast to hERalpha, ***hERbeta*** did not induce reporter activity driven by the hRARalpha-1 promoter in the presence of estrogen. While ***hERbeta*** did not confer estrogen responsiveness on this promoter, it did elicit transcriptional activation in the presence of 4-hydroxytamoxifen (4-OH-Tam). Additionally, this 4-OH-Tam agonist activity via ERbeta was completely blocked by estrogen. Like ERalpha, transcriptional activation of this promoter by ERbeta was not mediated by direct receptor binding to DNA. While hERalpha was shown to act through two estrogen-responsive sequences within the promoter, ***hERbeta*** acted only at the 3'-region, through two Sp1 sites, in response to 4-OH-Tam. Other ER antagonists including raloxifene, ICI-164,384 and ICI-182,780 also acted as agonists through ERbeta via the hRARalpha-1 promoter. Through the use of mutant and chimeric receptors, it was shown that the 4-OH-Tam activity via ERbeta from the hRARalpha-1 promoter in Hep G2 cells required the amino-terminal region of ERbeta, a region that was not necessary for estrogen-induced ERbeta activity from an ERE in Hep G2 cells. Additionally, the progesterone receptor (PR) antagonist RU486 acted as a weak ($IC_{50} > 1$ microM) antagonist via hERalpha and as a fairly potent (IC_{50} approximately 200 nM) antagonist via ***hERbeta*** from an ERE-driven reporter in cells that do not express PR. Although RU486 bound only weakly to ERalpha or ERbeta in vitro, it did bind to ERbeta in whole-cell binding assays, and therefore, it is likely metabolized to an ERbeta-interacting compound in the cell. Interestingly, RU486 acted as an agonist through ERbeta to stimulate the hRARalpha-1 promoter in Hep G2 cells. These findings may have ramifications in breast cancer treatment regimens utilizing tamoxifen or other ER antagonists and may explain some of the known estrogenic or antiestrogenic biological actions of RU486.

ACCESSION NUMBER: 1999094591 MEDLINE
 DOCUMENT NUMBER: 99094591 PubMed ID: 9879982
 TITLE: A novel human ***estrogen*** receptor*** beta: identification and functional analysis of additional N-terminal amino acids.
 AUTHOR: Bhat R A; Harnish D C; Stevis P E; Lytle C R; Komm B S
 CORPORATE SOURCE: Women's Health Research Institute, Wyeth-Ayerst Research, Radnor, PA 19087, USA.. bhatr@war.wyeth.com
 SOURCE: JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY, (1998 Nov) 67 (3) 233-40.
 Journal code: AX4; 9015483. ISSN: 0960-0760.
 PUB. COUNTRY: ENGLAND: United Kingdom
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199901
 ENTRY DATE: Entered STN: 19990202
 Last Updated on STN: 19990202
 Entered Medline: 19990121
 AB A novel human ***estrogen*** ***receptor*** beta (***hERbeta***) was cloned from human testis mRNA, ovary and thymus cDNA utilizing PCR and 5' RACE methods. The 5' end of ***hERbeta*** contained an additional open reading frame, in-frame and upstream of the published clones. ***hERbeta*** encodes a protein of 530 amino acids with an approximate molecular weight of 63 kDa and is larger than the previously reported rat, mouse and human protein. To determine the functional role of additional N-terminal amino acids, we compared the transcription functions of receptor lacking (hERbetaT) and receptor containing (hERbetaL) this N-terminal extension. hERbetaL is more active than hERbetaT in transactivating ERE-based reporter genes. hERbetaL, but not hERbetaT, attenuated cytokine mediated NFkappaB activation. Taken together, the additional N-terminal amino acids appear to play a role in modulating estrogen responsive gene expression in vitro.

L3 ANSWER 11 OF 13 MEDLINE
 DUPLICATE 7
 ACCESSION NUMBER: 1998139878 MEDLINE
 DOCUMENT NUMBER: 98139878 PubMed ID: 9473491
 TITLE: The complete primary structure of human ***estrogen*** receptor*** beta (***hER*** ***beta***) and its heterodimerization with ER alpha in vivo and in vitro.
 AUTHOR: Ogawa S; Inoue S; Watanabe T; Hiroi H; Orimo A; Hosoi T; Ouchi Y; Muramatsu M
 CORPORATE SOURCE: Department of Biochemistry, Saitama Medical School, Japan.
 SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1998 Feb 4) 243 (1) 122-6.
 Journal code: 9Y8; 0372516. ISSN: 0006-291X.
 PUB. COUNTRY: United States
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 OTHER SOURCE: GENBANK-AB006590
 ENTRY MONTH: 199803
 ENTRY DATE: Entered STN: 19980326
 Last Updated on STN: 20000303
 Entered Medline: 19980316
 AB Human ***estrogen*** ***receptor*** beta (***hER*** ***beta***) cDNA that encodes the full-length amino acid sequence has been isolated from testis poly(A)+ RNA with the combination of cDNA screening and reverse transcription-PCR. It is composed of a 1590-bp open reading frame and a segment of the 5'- and 3'-untranslated region (UTR) and encodes an additional 53 amino acids in the N-terminal region compared with the previously reported one. Protein interaction between ER alpha and ER beta was demonstrated in vitro by GST pull-down assay and in vivo by immunoprecipitation. Thus, this study indicates that ER alpha and ER beta can interact in vivo, cross-signaling each other.

ACCESSION NUMBER: 1998300286 MEDLINE
 DOCUMENT NUMBER: 98300286 PubMed ID: 9636657
 TITLE: Cloning and characterization of human ***estrogen*** receptor*** beta isoforms.
 AUTHOR: Moore J T; McKee D D; Slentz-Kesler K; Moore L B; Jones S; Horne E L; Su J L; Kliewer S A; Lehmann J M; Willson T M
 CORPORATE SOURCE: Department of Molecular Sciences, Glaxo Wellcome Research and Development, Research Triangle Park, North Carolina
 27709, USA.. jtm36008@glaxowellcome.com
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 ENTRY MONTH: 199807
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 AB Multiple transcripts which arise from the human ***estrogen*** receptor*** beta (ER beta) gene have been characterized. Three full length isoforms of the ***hER*** ***beta*** gene, designated ***hER*** ***beta*** 1-3, were identified in a testis cDNA library. An additional two isoforms, designated ***hER*** ***beta*** 4 and ***hER*** ***beta*** 5, were identified by PCR amplification from testis cDNA and from the MDA-MB 435 cell line. ***hER*** ***beta*** 1 corresponds to the previously described ***hER*** ***beta***. All five isoforms diverge at a common position within the predicted helix 10 of the ligand binding domain of ***hER*** ***beta***, with nucleotide sequences consistent with differential exon usage. The ***hER*** ***beta*** isoform mRNAs displayed a differential pattern of expression in human tissues and in tumor cell lines when analyzed by RT-PCR. Further characterization of the three full length isoforms, ***hER*** ***beta*** 1-3, by in vitro band shift studies indicated that the isoforms were able to form DNA-binding homodimers and heterodimers with each other and with the ER alpha subtype.

L3 ANSWER 13 OF 13 MEDLINE
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 ACCESSION NUMBER: 97467383 MEDLINE
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 TITLE: Human ***estrogen*** ***receptor*** beta binds DNA in a manner similar to and dimerizes with ***estrogen*** receptor*** alpha.
 AUTHOR: Pace P; Taylor J; Suntharalingam S; Coombes R C; Ali S
 CORPORATE SOURCE: Department of Medical Oncology, Imperial College of Medicine, Charing Cross Campus, St. Dunstan's Road, London W6 8RF, United Kingdom.
 SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Oct 10) 272 (41) 25832-8.
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 AB The cloning of a novel ***estrogen*** receptor*** beta (denoted ERbeta) has recently been described (Kuijper, G. G. J. M., Enmark, E., Pelto-Huikko, M., Nilsson, S., and Gustafsson, J.-A. (1996) Proc. Natl. Acad. Sci. U. S. A. 93, 5925-5930 and Mosselman, S., Polman, J., and Dijkema, R. (1996) FEBS Lett. 392, 49-53). ERbeta is highly homologous to

L3 ANSWER 10 OF 13 MEDLINE
 DUPLICATE 6

the "classical" ***estrogen*** ***receptor*** alpha (here referred to as ERalpha), has been shown to bind estrogens with an affinity similar to that of ERalpha, and activates expression of reporter genes containing estrogen response elements in an estrogen-dependent manner. Here we describe functional studies comparing the DNA binding abilities of human ERalpha and beta in gel shift assays. We show that DNA binding by ERalpha and beta are similarly affected by elevated temperature in the absence of ligand or in the presence of 17beta-estradiol and the partial estrogen agonist 4-hydroxy-tamoxifen. In the absence of ligand, DNA binding by ERalpha and beta is rapidly lost at 37 degrees C, while in the presence of 17beta-estradiol and 4-hydroxy-tamoxifen, the loss in DNA binding at elevated temperature is much more gradual. We show that the loss in DNA binding is not due to degradation of the receptor proteins. However, while the complete antagonist ICI 182, 780 does not "protect" human ERalpha (hERalpha) from loss of DNA binding at elevated temperature in vitro, it does appear to protect human ERbeta (***hERbeta***), suggestive of differences in the way ICI 182, 780 acts on hERalpha and beta. We further report that ERalpha and beta can dimerize with each other, the DNA binding domain of hERalpha being sufficient for dimerization with ***hERbeta***. Cell and promoter-specific transcription activation by ERalpha has been shown to be dependent on the differential action of the N- and C-terminal transcription activation functions AF-1 and AF-2, respectively. The existence of a second ***estrogen*** ***receptor*** gene and the dimerization of ERalpha and beta add greater levels of complexity to transcription activation in response to estrogens.